Predictors of Accidental Fatal Drug Overdose Among a Cohort of Injection Drug Users

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ABSTRACT

Objectives. This study evaluated factors associated with accidental fatal drug overdose among a cohort of injection drug users (IDUs).

Methods. In a prospective cohort study of 2849 IDUs in King County, Washington, deaths were identified by electronically merging subject identifiers with death certificate records. Univariate and multivariate Cox regression analyses were performed to identify predictors of overdose mortality.

Results. Thirty-two overdoses were observed. Independent predictors of overdose mortality were bisexual sexual orientation (relative risk [RR] = 4.86; 95% confidence interval [CI] = 2.30, 13.2), homelessness (RR = 2.30; 95% CI = 1.06, 5.01), infrequent injection of speedballs (RR = 5.36; 95% CI = 1.58, 18.1), daily use of powdered cocaine (RR = 4.84; 95% CI = 1.13, 20.8), and daily use of poppers (RR = 22.0; 95% CI = 1.74, 278).

Conclusions. Sexual orientation, homelessness, and drug use identify IDUs who may benefit from targeted interventions. (*Am J Public Health.* 2001; 91:984–987)

The association between injection drug use and increased risk of mortality has been previously documented.[1–4] Standardized mortality ratios have indicated that injection drug users (IDUs) are 6 to 20 times more likely to die prematurely than their peers.[1–4] Deaths due to accidental overdose are a major cause of mortality among IDUs.[3,5–8] Factors that increase the risk of fatal overdose include use of multiple drugs, temporal variations in the purity of drugs, and termination of methadone maintenance treatment.[4,9–11]

Since June 1994, the RAVEN Study, a cohort study of IDUs, has been conducted by Public Health—Seattle and King County. Vital status was recorded as part of assessing follow-up. Review of the death certificates of deceased subjects revealed that the largest proportion of deaths were due to accidental drug overdose. We attempted to identify the risk factors, based on baseline data, that are predictive of accidental fatal overdose. The results of toxicologic tests performed during autopsy are also presented.

Methods

The methods for the RAVEN Study have been described elsewhere.[12] All subjects injected drugs during the year prior to enrollment. At baseline, an interview was conducted and blood samples were obtained.

Vital status was ascertained by electronically merging RAVEN subjects' identifying information with computerized death certificates maintained by Public Health—Seattle and King County for all deaths recorded through March 18, 1997. Copies of the death certificates were obtained for all decedents who appeared to match a RAVEN subject on the basis of first name, surname, and age. After we obtained these death certificates, other data (e.g., the date and location of birth, mother's maiden name) from the 2 sources were examined for concordance. For deaths that reportedly occurred outside of King County, individual requests for copies of death certificates were made to the vital statistics offices in other jurisdictions. Identifying information for all RAVEN subjects was also electronically merged with computerized Washington State death certificates for the years 1994 through 1996. The matching criteria described above were used to identify RAVEN subjects among these death records.

Deceased subjects were classified as "accidental drug overdose" or "other" on the basis of the contents of the death certificate. Accidental (vs intentional) overdoses were those that lacked evidence of suicidal intent (i.e., no note left at the scene, no reports from others that the deceased was despondent, and no history of previous suicide attempts) (J. Nakagawara, MHA, oral communication, November 2000).

Excluded from analysis were 40 deceased subjects with other causes of death and 10 subjects who did not self-identify as heterosexual, gay, lesbian, or bisexual. Univariate and multivariate (stepwise forward selection) Cox regression analyses were performed to identify predictors of accidental overdose death. The final model contained age, sex, race/ethnicity, and those variables that either remained significant predictors of death after adjustment or appeared to confound the relationship between another variable and risk of mortality, as assessed by 10% changes in the risk coefficients. All analyses were performed with Stata for Windows (Stata Corp, College Station, Tex).

Results

Data from 2849 RAVEN subjects enrolled between June 1994 and March 1997 were used in these analyses. These subjects provided 4591 person-years of follow-up (mean = 1.6 years). Death certificates were obtained for the 72 subjects (2.5% of the cohort) who died prior to March 18, 1997.

TABLE 1—Selected Baseline Characteristics of the 2849 RAVEN Study Subjects[a]: Seattle–King County, Washington, 1994–1997

	Vital Status at End of Follow-Up					
	Alive (n = 2777)		Deceased (n = 72)		Deceased From Drug Overdose[b] (n = 32)	
Mean days of follow-up ± SEM (range)	595 ± 4.83 (1–1019)		343 ± 24.49 (4–805)		310 ± 34.96 (4–651)	
Mean age at interview ± SEM (range)	36.4 ± 0.16 (15–67)		39.0 ± 1.09 (21–64)		36.6 ± 1.40 (21–53)	
Mean years since first injection ± SEM (range)	15.7 ± 0.19 (0.0–53.2)		19.5 ± 1.29 (0.4–44.6)		17.8 ± 1.83 (0.4–39.1)	
	n	%	n	%	n	%
Sex						
Male	1751	63.1	47	65.3	23	71.9
Female	1026	36.9	25	34.7	9	28.1
Race/ethnicity						
White	1801	64.9	53	73.6	23	71.9
African American	616	22.2	10	13.9	4	12.5
Hispanic	126	4.5	1	1.4	1	3.1
Native American	120	4.3	3	4.2	2	6.3
Other	108	3.9	5	6.9	2	6.3
Primary drug injected						
Heroin	1808	65.1	40	55.5	19	59.4
Speedballs	410	14.8	11	15.3	4	12.5
Cocaine	326	11.7	14	19.4	7	21.9
Speed	165	5.9	5	6.9	2	6.3
Heroin and speed	5	0.2	0	0.0	0	0.0
Other opiates	6	0.2	1	1.4	0	0.0
Other drugs	6	0.2	0	0.0	0	0.0
Education						
Less than high school	720	25.9	16	22.2	9	28.1
High school graduate/GED	1090	39.3	30	41.7	12	37.5
Some college	836	30.1	21	29.2	10	31.3
College graduate	124	4.5	5	6.9	1	3.1
Residential status						
With a home	1702	61.2	35	48.6	11	34.4
Homeless	991	35.7	33	45.8	18	56.3
Self-reported sexual orientation						
Heterosexual	2498	90.0	57	79.2	25	78.1
Gay	52	1.9	3	4.2	1	3.1
Lesbian	24	0.9	0	0.0	0	0.0
Bisexual[c]	189	6.8	11	15.3	6	18.8
Ever in jail, prison, or juvenile detention						
No	268	9.7	7	9.7	1	3.1
Yes	2296	82.7	60	83.3	30	93.8
In jail, prison, or juvenile detention in last month (prior to baseline interview)						
No	1635	58.9	42	58.3	20	62.5
Yes	661	23.8	18	25.0	10	31.3
HIV antibody status						
Negative	2700	97.2	68	94.4	32	100
Positive	63	2.3	4	5.6	0	0
Hepatitis C antibody status						
Negative	481	17.3	16	22.2	9	27.3
Positive	2281	82.1	55	76.4	23	72.7

Note. SEM = standard error of the mean; GED = general equivalency diploma.
[a]Percentages may not total 100% because of missing values.
[b]Included in the total number (n = 72) of deaths.
[c]Includes men (n = 65) and women (n = 130). The 6 overdose deaths among this subgroup comprise 3 men and 3 women.

The cohort was 63% male and 65% White (Table 1). The mean age was 36.5 years (range = 15–67 years). The mean duration of injection drug use was 15.7 years. Heroin was the primary drug injected by the majority of subjects. Eighty-nine percent of all subjects were unemployed at baseline and 36% were homeless. About 10% of the cohort self-identified as a sexual minority. Over 80% reported prior incarceration. HIV seroprevalence was 2.4%. Prior infection with hepatitis B and hepatitis C was common. The all-cause mortality rate was 15.9 deaths per 1000 person-years.

In the multivariate analysis, 5 factors proved to be independent predictors of overdose mortality: bisexual sexual orientation (relative risk [RR] = 4.86), homelessness (RR = 2.30), less-than-daily injection of speedballs (injections of heroin and cocaine) (RR = 5.36), daily use of powdered cocaine (RR = 4.84), and daily use of "poppers" (defined as amyl nitrate, butyl nitrate, or other inhalants) (RR = 22.0) (Table 2). Two other factors that were predictive of overdose mortality in the univariate analysis—living alone and less-than-daily use of (noninjected) stimulants—failed to retain a significant association with this fatal outcome when adjustment was made for these other variables.

TABLE 2—Predictors of Death Due to Accidental Drug Overdose Among Injection Drug Users: Seattle–King County, Washington, 1994–1997

	n	Deaths	Person-Years at Risk	Mortality Rate[a]	RR (95% CI) (Univariate Analyses)	Adjusted RR (95% CI)[b,c] (Multivariate Analyses)
Sex						
Male	1774	23	2878	8.0	1.0	1.0
Female	1035	9	1671	5.4	0.68 (0.31, 1.46)	0.71 (0.29, 1.77)
Age (years)						
<25	250	1	411	2.4	1.0	1.0
25–34	874	11	1398	7.9	3.23 (0.42, 25.1)	5.29 (0.62, 45.5)
35–44	1262	14	2072	6.8	2.79 (0.37, 21.2)	4.06 (0.48, 34.4)
≥45	423	6	667	9.0	3.70 (0.45, 30.7)	7.38 (0.74, 73.3)
Race						
Non-White	985	9	1705	5.3	1.0	1.0
White	1824	23	2844	8.1	1.50 (0.69, 3.25)	1.44 (0.61, 3.40)
Sexual orientation						
Heterosexual	2523	25	4105	6.1	1.0	1.0
Gay	53	1	86	11.6	1.83 (0.25, 13.5)	3.54 (0.46, 26.9)
Bisexual	195	6	307	19.5	3.21 (1.32, 7.83)	4.86 (2.30, 13.2)
Living arrangement						
With others	1223	11	2137	5.1	1.0	
Alone	607	12	1005	11.9	2.28 (1.01, 5.17)	
Residential status						
With a home	1713	11	2759	4.0	1.0	1.0
Homeless	1009	18	1580	11.4	2.82 (1.33, 5.97)	2.30 (1.06, 5.01)
Injection Drug Use in Previous 6 Months						
Speedballs						
Never	977	3	1482	2.0	1.0	1.0
< Once/day	1115	21	1673	12.6	6.22 (1.86, 20.9)	5.36 (1.58, 18.1)
≥ Once/day	531	4	901	4.4	2.23 (0.50, 9.96)	1.98 (0.44, 8.99)
Cocaine						
Never	1215	7	1790	3.9	1.0	
< Once/day	1087	17	1625	10.5	2.45 (1.06, 5.69)	
≥ Once/day	319	3	562	5.3	1.27 (0.34, 4.80)	
Other Noninjection Drug Use in Previous 6 Months						
Cocaine						
Never	2166	20	3474	5.8	1.0	1.0
< Once/day	509	7	773	9.1	1.52 (0.64, 3.59)	1.37 (0.57, 3.31)
≥ Once/day	52	3	85	35.3	5.93 (1.76, 19.9)	4.84 (1.13, 20.8)
Stimulants						
Never	2372	22	3540	6.3	1.0	
< Once/day	294	7	427	16.4	2.60 (1.11, 6.05)	
Poppers						
Never	2662	29	4238	7.1	1.0	1.0
≥ Once/day	3	1	4	250	30.8 (4.19, 226)	22.0 (1.74, 278)

Note. RR = relative risk; CI = confidence interval.
[a]Deaths per 1000 person-years of follow-up.
[b]Each variable is adjusted simultaneously for all other variables in this column. Blank cells in this column represent variables that were not retained in the final model.
[c]Complete data were available for 2586 subjects, including 28 who died by accidental overdose.

All but 1 of the 32 overdose deaths occurred within King County, and autopsy results are available for 30 of these 31. The toxicologic data from the medical examiner's office indicate that 15 (50%) of these overdose victims tested positive for the metabolites of cocaine and of heroin or morphine. All 15 had injected the 2 drugs, which suggests that their deaths were due to speedballs. Of the remaining 15 for whom toxicologic data were available, 9 had positive results for heroin or morphine only, 1 had positive results for cocaine only, and 5 had positive results either for cocaine or for heroin or morphine in addition to another drug.

Discussion

Forty-four percent of the deaths observed among the RAVEN subjects were due to accidental drug overdose. This is consistent with other studies among IDUs, which have found that, even with the competing risk of HIV/AIDS, deaths due to accidental overdose remain a major cause of mortality.[3,5–8]

This study's limitations include possible incomplete ascertainment of deaths. Although our process of matching on personal identifier information served to identify virtually all deaths that occurred through March 18, 1997, in King County and through December 31, 1996, in the rest of Washington, it is likely that deaths occurring outside of the state went undetected. We also do not have data on incarcerations just prior to death, so we are unable to assess the previously observed association between recent release from incarceration and overdose mortality.[13] Finally, the short duration of follow-up limited the observation of deaths attributable to causes of mortality with long induction periods.

This study's strengths include the comprehensiveness of the standardized baseline interview, which covered factors such as sexual orientation and residential status that have rarely been evaluated for association with mor-

tality in studies involving IDUs. The relatively short duration of follow-up (mean=339 days) means that subjects' responses to the interview items about drug use in the previous 6 months are also likely to reflect their patterns of drug use at the time of their deaths. The inclusion of medical examiner data in these analyses allowed for the evaluation of concordance between a subject's self-reported drug use and the toxicologic evidence of drug use collected during the autopsy.

An important finding was that bisexual sexual orientation was predictive of death by overdose. Our study is the first to report this association, and the interpretation is unclear. The sociologic concept of social marginality—failing to find membership within a single socially recognized group—has previously been used to describe the sociologic position of bisexuals and may help to explain our findings.[14] Perhaps self-identified bisexuals feel like outsiders both among the heterosexual majority and within the gay and lesbian community. Feelings of isolation and loneliness may negatively influence mental health, leading to riskier drug-using behaviors and thereby increasing the risk of fatal overdose.

The association between homelessness and increased risk of death from overdose has not been reported previously and warrants further investigation. Homelessness may be the result of a more severe addiction, or more hazardous drug-using practices may be adopted as a way of coping with the physical and psychologic trauma of being homeless. Regardless of the direction of the relationship between homelessness and risky drug injection practices, this finding identifies a subgroup of IDUs that may benefit from targeted interventions.

The use of 2 types of noninjected drugs, powdered cocaine and poppers, was independently and strongly associated with the risk of overdose death. Previous studies have also cited use of multiple drugs as an important factor in deaths among IDUs, but much of this literature has focused on alcohol and other depressants (e.g., barbiturates and benzodiazepines) in conjunction with injected opiates.[4,8]

Recent infrequent injection of speedballs was an important predictor of fatal overdose. Toxicologic tests performed during autopsy seemed to confirm that speedball use played an important role in the fatal overdoses within this cohort. This is a noteworthy finding with implications for local public health interventions, given that overdose deaths involving heroin increased from 3.1 per 100000 to 6.6 per 100000 in King County from 1991 to 1999.[15] Our analyses indicate that focusing on heroin alone may miss half of the story. Although heroin was the most commonly injected drug among this cohort, it was the recent injection of heroin combined with cocaine that predicted fatal overdose.

Considering the drugs whose use independently predicted fatal overdose (powdered cocaine, poppers, and infrequent use of injected speedballs), the profile that emerges of the overdose victim is that of an IDU who pursues a "speedy," stimulated high rather than a sedated, sleepy high. It is unclear whether the observed relationship between these drugs and overdose mortality is due to drug interactions that increase the risk of mortality or whether these IDUs accidentally overdose on heroin while trying to "take the edge off" their stimulated highs.

We have identified accidental drug overdose as a major cause of mortality among IDUs in King County, Washington, and have identified independent predictors of fatal overdose. Educational and risk-reduction interventions targeted toward subgroups of the IDU population may be warranted. Future studies should seek to replicate these findings and gain further understanding of the observed relationships between sexual orientation and homelessness and the risk of overdose mortality as well as the specific mechanisms by which use of multiple drugs increases the risk of overdose. Studies that evaluate other factors closer in time to the actual overdose event may prove to be especially helpful in furthering our understanding of this fatal outcome. □

Contributors

P. T. O'Driscoll, J. McGough, C. Critchlow, and E. R. Alexander planned the analyses of the RAVEN data. J. McGough, H. Hagan, H. Thiede, and E. R. Alexander supervised the data collection. P. T. O'Driscoll analyzed the data. C. Critchlow and E. R Alexander supervised the data analyses. All authors contributed to the writing of the paper.

Acknowledgments

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